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VNUT is required for producing pain hypersensitivity after peripheral nerve injury

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Abstract

Neuropathic pain is one of the most debilitating pain syndromes, which occurs after several diseases accompanied by nerve damage such as diabetes or cancer. We have previously shown that activation of ATP-gated purinergic P2X4 receptor in the spinal cord, the expression of which is upregulated in reactive microglia following peripheral nerve injury (PNI), is crucial for the pathogenesis of neuropathic pain. However, the mechanism of ATP supply in the spinal cord remains unknown. In this study, we examined the role of vesicular nucleotide transporter (VNUT), a protein that accumulate ATP and other nucleotides in the secretory vesicles of cells. In the spinal cord of normal mice, VNUT expression was detectable but low; however, the expression of which was markedly increased in the ipsilateral spinal cord after PNI. Interestingly, knockdown of VNUT expression by spinal administration of small interference RNA alleviated pain hypersensitivity after PNI. Together, these findings suggested that the VNUT may play an important part in forming ATP-enriched vesicles crucial for generating neuropathic pain.